

REMARKS

The present application is directed to therapeutic delivery compositions and methods that are particularly suited for the effective delivery of genetic matter and compounds to the interior of cells. Following entry of this amendment Claims 1-42 will be pending. Claims 1, 8-9, 16-17, 19, 26-27, 33, 38 and 41 are amended herein. No new matter is added and support for the amendments is found throughout the specification.

Claim Objection.

In the Office Action mailed June 2, 2004, the Examiner objected to Claims 33 and 38 on the basis that they were grammatically incorrect. Applicants have amended Claim 33, line 2, to remove the extra word "a" in line 2, as suggested by the Examiner and have amended Claim 38, line 3, to replace the phrase "a gene products" with "a gene product". Applicants respectfully submit that the amendments to the claims overcome the Examiner's objection.

Priority

In the Office Action mailed June 2, 2004, the Examiner rejected applicants' priority claim to U.S.S.N. 08/138,271 (hereinafter the '271 application) and U.S.S.N. 07/673,289 (hereinafter the '289 application). In particular, the Examiner stated that neither priority document **alone** provided support for the combination of octablock copolymers and nucleic acids. Furthermore, the Examiner stated, "Applicants provide *no evidence or logic* to indicate that the '271 application relied upon Schmolka for its disclosure of octablock copolymers."*(emphasis added)*. Applicants respectfully disagree.

The scientific publication of Schmolka *et al.* (*J. Am. Oil Chemist Soc.* 54:110-116 (1977), hereinafter "Schmolka *et al.*") was incorporated by reference into both the '271 application (see page 21 and 23) and the '289 application (see page 23, lines 13-17). Schmolka *et al.* teach the synthesis of block polymer non-ionic surfactants **including octablock copolymers**, as shown in Figure 4 of the publication.

The '271 application describes copolymers in combination with nucleic acid sequences. At the time of filing, applicants were aware that Schmolka *et al.* taught the synthesis of several polymers. Accordingly, the '271 application incorporated the Schmolka *et al.* publication to provide disclosure for both linear **and** octablock copolymers in combination with nucleic acids. It was apparent to applicants at the time of filing the '271 application that their invention included the combination of linear polymers and nucleic acids **as well as** the combination of **octablock** copolymers and nucleic acids. Therefore, applicants were careful to incorporate into the '271 application a reference that taught **both** types of copolymers.

Applicants respectfully submit that other patent applicants have also referenced the Schmolka *et al.* publication to describe octablock copolymers and their synthesis. (For example, see formula XVII of U.S. Patent Nos. 6,440,743 and 5,656,611 to Kabanov *et al.*, which were cited by the Examiner.)

Applicants respectfully submit that the '271 application discloses nucleic acid sequences in combination with either linear polymers or octablock copolymers and therefore correctly claims priority for the presently claimed combination. Accordingly, applicants respectfully request a priority date of at least October 15, 1993.

Claim rejections under 35 U.S.C. § 112, 2nd paragraph

In the Office Action mailed June 2, 2004, the Examiner rejected Claims 1-42 under 35 U.S.C. 112, second paragraph, as being indefinite. The Examiner stated that use of the word "to" in a range of percentages rendered the claims indefinite. Applicants have amended all relevant claims to replace the word "to" with the word "and" in each range of percentages. Accordingly, applicants respectfully submit that the rejection under 35 U.S.C. 112, second paragraph, has been overcome and request its withdrawal.

Claim rejections under 35 U.S.C. § 102

In the Office Action mailed June 2, 2004, the Examiner rejected Claims 1-5, 8-13, 16-23, 26-31, 33-36, 38 and 41 as anticipated by Lemieux *et al.*, U.S. 6,359,054 (hereinafter "Lemieux

et al.”) under 35 U.S.C 102(e). The Examiner stated that Lemieux *et al.* teach methods of delivering to an animal a composition comprising octablock copolymers and nucleic acids. Applicants traverse the rejection.

Applicants respectfully submit that Lemieux *et al.* is an invalid 102(e) reference. As discussed above, the present application is entitled to a priority date of at least October 15, 1993. Therefore, applicants respectfully request withdrawal of the rejection under 35 U.S.C. 102(e).

In addition, applicants submit that the Lemieux *et al.* fail to disclose the molecular weight ranges of the copolymers as claimed. The Examiner asserts that Lemieux *et al.* disclose octablock copolymers T1101, T1301, T1501, T110R1, T130R1 and T150R1 and that these copolymers exhibit the claimed molecular weight range. However, applicants submit that Lemieux *et al.* recite an **average** molecular weight in the absence of standard deviations. Therefore, the molecular weight for each copolymer disclosed by Lemieux *et al.* is entirely unclear. The Examiner agrees that Lemieux *et al.* fails to define the term “about”. However, the Examiner proceeds to give the term “about” its broadest interpretation. Applicants respectfully submit that no support is provided in the Lemieux *et al.* specification to expand the molecular weight ranges to encompass the polymer molecular weight ranges specified in the present claims.

Therefore, applicants respectfully submit that Lemieux *et al.* is not a valid anticipatory reference and, even if it were, does not recite **all** the limitations of the claims. Accordingly, applicants respectfully submit that the rejection has been traversed and request its withdrawal.

Claim rejections under 35 U.S.C. § 103

In the Office Action mailed June 2, 2004, Claims 1, 6, 7, 9, 14, 15, 19, 24-25, 27, 32, and 37 were rejected under 35 U.S.C. 103(a) as obvious over Lemieux *et al.* in view of Emanuele *et al.* U.S. 5,674,911 (hereinafter “Emanuele *et al.*”). Applicants respectfully traverse.

Although Lemieux *et al.* fails to teach a composition containing both 0.1-5% by weight of a surfactant and 0.5-5% by volume of a low molecular weight alcohol, the Examiner asserts that Emanuele *et al.* teach that surfactants such as Tween 80 and ethanol may be added to emulsions of non-ionic block polymer compositions containing nucleic acids, (see col. 11, lines

39-58) and concludes that it would have been obvious to one skilled in the art to add surfactants and low molecular weight alcohol to the composition of Lemieux *et al.* in order to stabilize the emulsions.

Applicants respectfully submit that Lemieux *et al.* and Emanuele *et al.* are not valid prior art references because they were both filed after the priority date of the present application as described above. Applicants respectfully submit that the priority of the present application of at least October 15, 1993 overcomes the rejection under 35 U.S.C. 103(a) and request its withdrawal.

Claims 1, 2, 5, 8, 17-20, 23, 26 and 41 were rejected under 35 U.S.C. 103(a) as obvious over Pahlson *et al.* (*Acta Pathol. Microl. Immunol. Scand. B.* (1986)) (hereinafter "Pahlson *et al.*") in view of Woodard *et al.* (*Laboratory Animal Science* (1989)) (hereinafter "Woodard *et al.*"). The Examiner stated that Pahlson *et al.* teach a method of inducing an immune response in a mouse by administering whole bacteria emulsified in Freund's complete adjuvant. The Examiner stated that whole bacteria are considered to include expression vectors having sequences that can alter the function of nucleic acids. Further, whole bacteria would also be considered to comprise ribozymes, as part of their ribosomes, as well as antisense oligonucleotides. Pahlson *et al.* do not teach octablock copolymers. In addition, the Examiner stated that Woodard *et al.* teach that the octablock copolymer T1501 is equivalent to Freund's complete adjuvant for the purpose of stimulating antibody production. Therefore, the Examiner concluded it would be obvious to substitute the T1501 octablock copolymer of Woodard *et al.* for the Freund's complete adjuvant of Pahlson *et al.* to stimulate antibody production. Applicants respectfully traverse the Examiner's rejection.

It is well established in the art (see the Schmolka *et al.* publication) that the physical properties of block copolymers depend upon variations in the hydrophobe molecular weight and variations in hydrophile-hydrophobe balance. These are shown to be similar in each series of block copolymers (e.g. Pluronic, Tetronic, Pluradot and Pluronic-R) but differ from one copolymer (e.g. T1301) to the next, in any one series (e.g. T1501). For instance, increasing the overall percentage of POP in the total octablock copolymer results in an increase in the

hydrophobicity of the molecule and therefore an overall decrease in its water solubility. Similarly, if the percentage of POE increases over the total weight of the octablock copolymer then the solubility of the molecule will also increase. Applicants respectfully submit that the functionality of the block copolymers cannot be construed as equivalent amongst any one series (e.g. Tetronic). Thus, the invention as a whole could not be considered *prima facie* obvious because one skilled in the art would not have been motivated to substitute the T1501 octablock copolymer of Woodard *et al.* for the Freund's complete adjuvant of Pahlson *et al.* because such a substitution would have an impact on physical and biological interactions, and at the very least affect the characteristics of the block copolymer.

Claims 3, 4, 9-13, 16, 21-22, 27-31, 33, 35-36 and 38 were rejected under 35 U.S.C. 103(a) as obvious over Pahlson *et al.* and Woodard *et al.* as applied to Claims 1, 2, 5, 8, 17-20, 23 and 26 above, and further in view of U.S. Patent No. 4,902,500 to Jansen *et al.* (hereinafter "Jansen *et al.*").

The Examiner stated that it would have been obvious to substitute the T1301, T1101, T150R1, T130R2 and T110R1 of Jansen *et al.* for Freund's complete adjuvant. Applicants respectfully traverse the Examiner's rejection.

As stated above, it is well established that the physical properties of block copolymers depend upon variations in hydrophobe molecular weight and variations in hydrophile-hydrophobe balance. In addition, Jansen *et al.* describe stable antibody preparations containing a mixture of at least one polyoxypropylene-polyoxyethylene block copolymer **and at least one phospholipid**. Applicants' pending claims are directed to compositions containing octablock copolymers and one or more nucleic acid sequence. Applicants' composition and method do not require a phospholipid. Therefore, Applicants respectfully submit that Jansen *et al.* fail to teach or suggest the claimed compositions.

Claims 1-5, 8-13, 16-18, 20-22, 28-30 and 34-36 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kabanov *et al.* (U.S. Patent, 5,656,611). The Examiner stated that Kabanov *et al.* teach compositions comprising polynucleotide and octablock compositions having molecular weights and relative amounts of POP and POE overlapping the instant claims.

(abstract, col. 7, lines 23-col 8, line 11). The Examiner concluded that the claimed invention as a whole was *prima facie* obvious because the molecular weight ranges specified by the current application would have been obvious to one skilled in the art at the time of the invention. Applicants respectfully traverse the Examiner's rejection.

As described above, applicants submit that they disclosed the claimed limitations in the referenced priority documents, 08/138,271 and U.S.S.N. 07/673,289 and are entitled to a priority date of at least October 15, 1993. As such, Kabanov *et al.* is not a valid prior art reference and cannot be used to establish a case of *prima facie* obviousness.

Furthermore, Kabanov *et al.* claim polynucleotide compositions containing a polynucleotide or nucleic acid molecule which has been covalently modified, an octablock copolymer, **and** at least one polycation segment, which is a cationic homopolymer, copolymer, or block copolymer that is the reaction product of at least three amino containing monomers, or quaternary salts thereof, as demonstrated in Example 11. In contrast, applicants' compositions do not require at least one polycation segment, which is a cationic homopolymer, copolymer, or block copolymer that is the reaction product of at least three amino containing monomers, or quaternary salts thereof.

Claims 17, 39-40 and 42 were rejected under 35 U.S.C. 103(a) as obvious over Lemieux *et al.* Applicants respectfully traverse the rejection and repeat that Lemieux *et al.* is not a valid 35 U.S.C. 103(a) reference due to applicants' priority date of at least October 15, 1993.

In addition, as mentioned above, Lemieux *et al.* recite copolymers having an average molecular weight. However, because no standard deviation is provided, the molecular weight for each copolymer is entirely unclear and there is no support in the specification of Lemieux *et al.* to expand the molecular weight ranges to those specified in the present claims. Furthermore, the physical properties of block copolymers depend upon variations in hydrophobe molecular weight and variations in hydrophile-hydrophobe balance, and applicants submit that the functionality of block copolymers cannot be construed as equivalent amongst any one series (e.g. Tetronic).

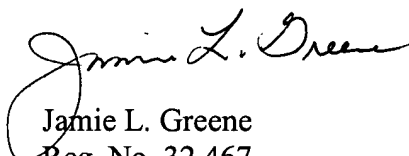
Accordingly, for the foregoing reasons, applicants respectfully request the withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

The foregoing is submitted as a full and complete response to the Office Action mailed on June 2, 2004. No new matter is added by these amendments. For at least the reasons given above, applicants respectfully submit that the pending claims are enabled, fully described, definite, novel and non-obvious. Accordingly, applicants submit that the claims in the present application are in condition for allowance, and such action is courteously solicited. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 11-0855.

The Examiner is invited and encouraged to contact the undersigned attorney of record at telephone number listed below if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,


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